A Trial of ExSept® for Hemodialysis Central Venous Catheters

Colleen Marie Astle
Louise Jensen

Central venous catheters (CVCs) are increasingly used for vascular access in hemodialysis patients. One of the major complications of CVCs is infection. The purpose of this randomized clinical trial was to determine if ExSept® was as effective as Chlorhexidine in reducing skin colonization, exit site, and central venous catheter-related blood stream infections. Patients with new dialysis catheters (n=121) were randomly assigned to the Chlorhexidine group or the ExSept® group. The duration of the study was 3 months per patient or until the development of an infection. Major outcome observations of the study were: 10 exit site infections (5 per group), 2 episodes of bacteremia (1 in the Chlorhexidine group and 1 in the ExSept® group), and 91.7% skin colonization. The conclusions drawn from this study are that infection rates were low in this cohort and ExSept® and Chlorhexidine had comparable efficacy.

The use of a central venous catheter (CVC) for either temporary or chronic hemodialysis has become an acceptable bridge to internal, permanent vascular access (Farrell, Walshe, Gellens, & Martin, 1997; Brunier, 1996; Ouwendyk & Helferty, 1996; Choudhury, Ahmed, Girgis, & Kronfli, 1999; Berkoben & Schwab, 1995; Tanriover et al., 2000; Rocklin, Dwight, Callen, Bispham, & Spiegel, 2001). Despite the consensus that the construction of primary arteriovenous (AV) fistulae represents the best choice for permanent vascular access, the trend since 1980 has been a continual increase in the use of CVCs because they are convenient and readily available. Kapoian and Sherman (1997) reported a 5% use of CVCs in 1980 that increased to 30% in 1993. CVCs are inserted into deep veins such as the subclavian, jugular, or femoral veins and are advanced into the vena cava (Brunier, 1996). They may be placed percutaneously or using a cutdown technique. Maturation time is not required; rather they may be used immediately after radiological verification of placement (Farrell et al., 1997; Chopra, 2001). CVCs are easily inserted with radiological fluoroscopic guidance or at the bedside, thereby reducing the need for expensive and often times unavailable operating room time. They can provide long-term access in children, the elderly, morbidly obese patients, or in patients with diabetes whose vessels are not acceptable for the creation of an internal fistula or graft (Rocklin et al., 2001). They are necessary for patients requiring emergency dialysis or patients who are described as access failures, having used up the vessels required to create a permanent access. CVCs serve as a backup for the fistulae and grafts that require ligation due to high output failure states and steal syndrome. Further, CVCs are inserted as a temporary access while awaiting the development of a permanent access.

The survival rates of CVCs are reported to be 75% at 1 year and 50% at 2 years, thereby allowing CVCs to become alternate forms of long-term accesses (Berkoben & Schwab, 1995; Parker, 1998; Rocklin et al., 2001). The disadvantage associated with the use of these catheters is that they offer lower blood flow rates than other accesses. Associated complications include central vein stenosis, thrombosis, and infection (Choudhury et al., 1999; Johnson, 1998; Maki, 1991; Taylor et al., 1998; Rocklin et al., 2001). Infection related to these devices results in significant increases in cost and morbidity (Gaynes, 2001). There are many potential targets for intervention aimed at reducing the incidence of catheter-related infection, including: hand washing, use of appropriate barrier precautions, insertion techniques, ointments, dressings, and antiseptics. Presently, povidine-iodine and Chlorhexidine are the two antiseptics used both at the time of insertion and during catheter maintenance. Electrolytic chloroxidizer (EC), commonly known as ExSept® is a chlorine-based solution composed of sodium hypochlorite and sodium chloride. ExSept® has been used for many years, to externally and internally clean dialysis machines (50% concentration), and as an antiseptic in the peritoneal dialysis population (50% concentration); however, it has not been considered as a hemodialysis skin and catheter antiseptic until recently (10% solution). Despite a lack of scientific evidence, a number of Canadian dialy-

***Colleen Marie Astle, MN, RN, CNeph(C), EPN**, is Dialysis Access Coordinator, Nephrology Nurse Practitioner, University of Alberta Hospital, Edmonton, Alberta, Canada.*

***Louise Jensen, RN, PhD**, is Professor, Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada.*

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sis units are presently using ExSept®. The question arises, how would ExSept® 10% compare to Chlorhexidine as a skin and hub antiseptic solution?

Background

Hospitalized patients frequently develop nosocomial infections that are caused by normal flora colonizing the patient at the time of admission, or by exogenous pathogens that are acquired and subsequently colonize the patient after admission to the hospital (Boyce, 1996). Approximately 200,000 nosocomial blood stream infections occur each year in the United States. Most of these infections are related to the use of intravascular devices (Gaynes, 2001). Maki (1991, 1992) has estimated that 90% of intravascular device-related blood stream infections are secondary to CVCs. Although new dialysis patients should have a functioning fistula upon entry into the hemodialysis unit, frequently a CVC is placed, predisposing an immunocompromised patient to the possibility of a local or systemic catheter-related infection (Zeylemaker, Jaspers, Van Kraaij, Visser, & Hoepelman, 2001).

In the guidelines for prevention of intravascular device-related infections prepared by the Centers for Disease Control and Prevention (CDC, 2002), catheter-related infections can be described as a colonized catheter, exit site infection, tunnel infection, catheter-related blood stream infection, and infusate-related bloodstream infection. A colonized catheter infection is described as the growth of greater than 15 colony-forming units (cfu) (semiquantitative culture) or 10^3 cfu (quantitative culture) from a proximal or distal catheter segment in the absence of accompanying clinical symptoms (Maki, 1992). A local catheter-related infection might comprise an exit site infection or a tunnel infection. The CDC Guidelines (2002) describe an exit-site infection as inflammation around the insertion site that consists of erythema, warmth, tenderness, induration, or purulence within 2 centimeters (cm) of the skin at the exit site of the catheter. The incidence of exit site infections range from 1.2 to 2.2 per 1000 catheter days (Saad, 2001). They may result from inadequate skin disinfection at the time of catheter placement, incorrect suture material or technique, improper site care by dialysis staff, or poor patient hygiene. A pocket infection is erythema and necrosis of the skin over the reservoir of a totally implantable catheter, or purulent exudate in the subcutaneous pocket containing the reservoir. A tunnel infection is characterized by erythema, tenderness, and induration in the tissues overlying the catheter more than 2 cm from the exit site. Tunnel infections are relatively uncommon with an incidence of 0.12 per 1000 catheter days (Saad, 2001).

Systemic catheter-related bacteremia has often been used as a diagnosis of exclusion to describe a bloodstream infection caused by an organism from the skin of a patient with a vascular catheter who has clinical manifestations of sepsis and no apparent source for the infection except the catheter. The implicating evidence is isolation of the same organism from a culture of a catheter segment and from the blood of a patient, with accompanying clinical symptoms of blood stream infection and no other apparent source of infection. In the absence of laboratory confirmation, if there is resolution of clinical sepsis within 48 hours of catheter removal during which time the patient does not receive antibiotics, the catheter is implicated as the source of infection. The patient may present with signs and symptoms of systemic infection ranging in severity from minimal to life-threatening. Fever and shaking chills are typical. Nausea, vomiting, back pain, headache, myalgia, arthralgia, and changes in mental status can also occur. The patient may develop hypotension. Some patients present to the dialysis unit with little or no evidence of infection and then develop symptoms after initiation of dialysis via the CVC, suggesting a release of bacteria or endotoxin from a sequestered source (Saad, 2001). Infectious complications of CVC associated bacteremia may include osteomyelitis, endocarditis, epidural abscess, septic arthritis, or death (Tanriover et al., 2000; Saad, 2001). The incidence of tunneled, cuffed catheter bacteremia was reported to be 1.2 episodes per 100 patient months (Marr et al., 1998). Saad (2001) and Tanriover et al. (2000) reported catheter-related infections of 3.4 to 5.5 episodes per 1000 catheter days. Oliver, Callery, Thorpe, Schwab, and Churchill (2001) related that temporary internal jugular catheters show a marked increase in rates of bacteremia 3 weeks following insertion. The episodes of bacteremia followed the occurrence of exit site infections.

Infusate-related bloodstream infection is defined as isolation of the same organism from infusate and from separate percutaneous blood cultures, with no other identifiable source of infection (Greene, 1996). These infections are rare but easily identified. They should be suspect when sepsis occurs in an otherwise low-risk patient receiving an intravenous solution, or when there is a cluster of primary bloodstream infections with an unusual organism. Organisms may contaminate infusate by several mechanisms: during manufacture, solution preparation, handling by health care workers or by retrograde contamination from a contaminated catheter (Gaynes, 2001).

Skin cleansing of the insertion site is regarded as one of the most important measures for preventing catheter-related infection. Historically, povidine-iodine is an antiseptic that has been used during the insertion and maintenance of the intravascular devices. It works by penetrating the cell wall of the microorganism. More recently, Chlorhexidine has been studied and found to be more effective as a skin antiseptic to prevent catheter-related infection (Mimoz et al., 1996;

Garland et al., 1995). It works in less time, retains its antibacterial against flora longer, is not inactivated by the presence of blood or human protein, and causes minimal skin irritation (Maki, 1991; Gaudet & Beaufoy, 1996; Mimoz et al., 1996; Dickenson, 1997). Chlorhexidine works by disrupting the microbial cell wall. It is active against many gram-positive and to a slightly lesser degree gram-negative bacterium. Electrolytic chloroxidizer, otherwise known as ExSept® is a chlorine-based solution with a 17% sodium chloride component and 0.057% sodium hypochlorite. ExSept® is a 10% solution. It is said to be effective against all spectrums of pathogens, including gram-positive, gram-negative, viruses and spores (Carter, 1995).

Purpose of the Study

The purpose of the study was to determine whether ExSept® 10% is as effective as the standard skin and hub antiseptic solution of Chlorhexidine 0.5% with 70% alcohol in decreasing the central venous catheter-related exit site infections in long-term, maintenance hemodialysis patients over a 3 month period. The hypotheses tested were:

1. There will be a decreased number of localized CVC exit site infections in the experimental group receiving ExSept® 10% than the control group receiving Chlorhexidine 0.5% with 70% alcohol.
2. There will be a decreased number of catheter-related blood stream infections in the experimental group receiving ExSept® 10% than the control group receiving Chlorhexidine 0.5% with 70% alcohol.
3. There will be decreased catheter colonization as measured by semiquantitative methods in the experimental group receiving ExSept® 10% than the control group receiving Chlorhexidine 0.5% with 70% alcohol.

Definition of Outcomes

Exit Site Infection (local): purulent discharge at the exit site or/tenderness, erythema with induration of ≥2 centimeters (cm) around the exit site, with a positive culture of serous discharge. Confirmed with a swab of the catheter exit site (APIC, 2000).

Skin Irritation: Reddened area covering the area where skin had previously been cleansed with antiseptic, approximately 5 cm x 5cm.

Catheter-Related Bacteremia: Two or more positive blood cultures with no evidence for source other than the catheter, or single positive blood culture and positive culture of catheter segment with identical organism, or single positive blood culture and positive culture from discharge from exit site with identical organism (APIC Text, 2000).

Central Venous Catheter Colonization: An intermediate value of greater than 15 colony-forming units (cfu) on roll plate culture represents a positive colonization obtained from skin swabs, intraluminal brushings and/or catheter tips (CDC, 2002).

Methods

Design

A randomized clinical trial with repeated measures was used to examine the effect of ExSept® on infection rates in patients with end stage renal disease (ESRD) using central venous catheters (CVCs) as their dialyzing access. The control group used the standard Chlorhexidine 0.5% with 70% alcohol as the catheter exit site and hub antiseptic and the treatment group used ExSept® 10% on the skin and 50% on the hub (ExSept® concentrations were based on recommendations by Alcavis International Inc.). The presence of exit site infection and catheter-related bacteremia were the primary outcome variables. Exit site skin colonization was the secondary outcome variable. Signs and symptoms of infection were monitored from the time of catheter insertion, at each dressing change to the end point of the study, which was the development of a catheter-related bacteremia or termination of the study at 3 months post-catheter insertion. Catheter brushings were done part way through the study period on a convenience sample of patients and exit site swabs were collected monthly on each patient.

Sample

The convenience sample consisted of new patients with ESRD who were initiated on hemodialysis, or who required a new CVC inserted and were currently receiving hemodialysis, were infection free, and were 18 years or older. The patients excluded were those who were not of legal age for consent, those with a confirmed infective process, carried methicillin resistant *Staphylococcus aureus* (MRSA) positive nasal swabs, or had an allergy to either study antiseptic solution.

Data Collection Protocol

Ethical approval for the study was attained from the Health Research Ethics Board. Patients were approached in the Incenter Hemodialysis Unit by the researcher on the day of their CVC insertion and the study explained. An informed consent was then obtained from patients willing to participate in the study. ExSept® is reported to be non-toxic and non-irritating. An allergic reaction to any drug product was considered. Observation of the patient's skin was to be monitored 3 times weekly for a skin rash covering the area of skin where the ExSept® was applied as well as for signs of infection. In the event of a catheter-related infection, the patient was treated with the appropriate antibiotics.

A package containing the data collection sheet and group assignment was selected. (All packages were previously prepared and randomly organized). The researcher completed the demographic information sheet. Nasal swabs were carried out on each patient to determine the presence of MRSA and

Staphylococcus carrier status, as those patients who are MRSA carriers are at greater risk for colonization of the skin and developing infection (Hoen, Paul-Dauphin, Hestin, & Kessler, 1998). One of three experienced nephrologists inserted the CVC, using the same method of insertion (Seldinger). The catheters were soft, dacron-cuffed, polyurethane, dual lumen catheters (Cardiomed ®) used for long-term maintenance hemodialysis.

One to 2 days following the CVC line insertion, at the time of the first hemodialysis treatment, and thereafter three times per week, the catheter dressing was removed and the exit site observed for signs of infection by a hemodialysis nurse. One of two randomly assigned antiseptics was used as per the hospital-approved procedure for care of the CVC and initiation of the dialysis procedure. Polysporin triple therapy antibiotic ointment (Taro Pharmaceuticals Inc.) was used consistently on the exit sites during the study. The ointment was removed prior to obtaining the skin swab. Once per month, for 3 months, swabs were taken of the catheter exit sites. Brushings (Endoluminal Catheter Brush, IDI Technologies, Ltd.) from the internal lumens of the catheters were obtained at the middle of the study period on a convenience sample of patients (11%) to determine endoluminal catheter colonization. In the event of clinical signs of infection, exit site skin swabs and blood cultures were drawn and appropriate antibiotic therapy instituted as required by standard practice in the unit. In the event of CVC removal, the catheter tip was to be collected and sent to the laboratory to be analyzed for colonization of microorganisms. The end point of the study was a confirmed catheter-related bacteremia or termination of the study at 3 months.

Data Analysis

Descriptive statistics were used to describe the sample characteristics and outcome variables. To determine the difference between the treatment and control groups on the number of exit site infections, rate of bacteremia, and exit site skin colonization, Chi-square analysis was conducted. Associations were also examined among catheter-related infection rates and patient demographics such as age, gender, cause of renal failure (diabetes mellitus), and serum albumin levels.

Findings

Characteristics of the Sample

There were 136 patients approached to participate in the study, with 121 patients being enrolled. The primary reason for refusal to participate was related to the length of time required to stay in the study. The patients who were being transferred to peritoneal dialysis within 3 months, being prepared for transplant, or those who could not commit to 3 months were not enrolled. One patient was not interested and one Nephrology Fellow was late in becoming involved in the study, therefore those patients were not enrolled in the study. Each patient's progress was tracked for 3 months, 36 dialysis treatments, or 90 catheter days. The cumulative study time for 121 patients was 10,890 catheter days (5,445 days per group), 363 patient months, or 4,356 treatments.

The final sample consisted of 103 patients, as 18 patients did not complete the study (14.87%). Seven patients died during the study (5.78%). Causes of death were listed as peritoneal failure that subsequently developed into a peritonitis (n=1), cardiac arrest secondary to cause unknown in two patients (n=2), myocardial infarction (n=1), ischemic gut secondary to cardiovascular disease (n=1), cardiac arrest secondary to aortic dissection (n=1), and hemothorax secondary to catheter insertion (n=1). Two patients required hernia repair associated with peritoneal dialysis and were to be supported by hemodialysis for 12 weeks but returned to peritoneal dialysis earlier than anticipated. Two patients recovered kidney function and were discharged from the program. One patient received a cadaveric transplant. Two patients related that the smell of the ExSept® solution made them nauseated. Turning their faces away or wearing masks did not alleviate the problem. One patient's CVC fell out. Rather than replacing the catheter, the AV graft was used earlier than was planned. One patient who had developed skin cancer secondary to immunosuppressive therapy subsequent to a renal transplant found the ExSept® solution irritating to the skin. One patient decided to discontinue dialysis and leave the treatment program. One patient who had emotional issues to deal with felt he could not cope with continued participation in the study.

Patient randomization to the two treatment groups was as follows: 64 (52.9%) to the Chlorhexidine group and 57 (47.1%) to the ExSept® group. Table 1 illustrates the demographic characteristics of the sample. Overall, the patients ranged in age from 18 to 70 years (M±SD = 63.18 ± 15.47). The mean age for the Chlorhexidine group was 63.28 ± 15.23 years and 63.07 ± 15.87 years for the ExSept® group ($t = .075$, $p=.882$).

Exit Site Infections

The first hypothesis was to compare two skin and hub antiseptics on rates of exit site infections. Of the 121 patients participating, 10 patients (8.26%) developed exit site infections; 5 were from each group (see Table 2). Though infections are a serious complication associated with CVCs, the incidence in this study was relatively low (.91/1000 catheter days).

Bacteremia Rates

The second hypothesis studied was the effect of the antiseptics on bacteremia, which was confirmed by the presence of a positive blood culture and the presence of symptoms. Two bacteremic episodes occurred in

Table 1
Characteristics of the Subjects

Characteristic	Group		
	Chlorhexidine 64	ExSept® 57	*p* value
Age (years, M±SD)	63.28 ± 15.23	63.07 ± 15.87	.882
Gender			.103
Male [n(%)]	39 (60.93%)	26 (45.61%)	
Female [n(%)]	25 (39.07%)	31 (54.39%)	
Height (cm, M±SD)	165.03 ± 11.34	163.30 ± 13.69	.447
Weight (kg, M±SD)	73.18 ± 20.14	74.04 ± 17.95	.972
BMI (m^2, M±SD)	27.25 ± 7.48	27.70 ± 5.88	.547
Albumin (g/L, M±SD)	32.08 ± 5.49	31.26 ± 5.63	.751
Immunosuppressed [n(%)]	7 (10.93%)	3 (5.26%)	.213
Disease			.464
Diabetic Nephropathy	29 (45.31%)	21 (36.84%)	
Other	14 (21.88%)	19 (33.33%)	
Glomerulonephritis	10 (15.62%)	4 (7.02%)	
Hypertension	6 (9.38%)	6 (10.53%)	
Unknown	4 (6.25%)	6 (10.53%)	
Renal Vascular Disease	1 (1.56%)	1 (1.75%)	

Table 2
Exit Site Infections

Exit Site Infections	Group (n)		Total	*p* value
	Chlorhexidine	ExSept®		.553
Negative culture	59	52	111	
Clinical signs and positive culture	3	5	8	
Clinical signs	2	0	2	
Total	64	57	121	

Table 3
Bacteremic Episodes

Culture Results	Group (n)		Total
	Chlorhexidine	ExSept®	
Positive	1	1	2
Negative	61	56	117
Possible*	2	0	2
Total	64	57	121

*Not confirmed by culture

this study, one from each group (see Table 3). Though only 13 catheter brushings were performed, one brushing did grow Coagulase-negative Staphylococcus. This patient did not develop a bacteremia.

Skin Colonization

The third hypothesis studied was that skin colonization would be reduced by the skin and hub antiseptic, ExSept®. However, 111 (91.7%) of the 121 patients had colonization of the skin surrounding the exit sites; 56 patients in the Chlorhexidine group and 55 in the ExSept® group (see Table 4). Of the 10 exit site infections, all had colonization of the skin surface.

Factors Affecting Catheter-Related Infections

It is well documented in the literature that infection is a frequent occurrence in patients with ESRD receiving hemodialysis (Marr et al., 1997). Several factors have been associated with catheter-related infections. Powe, Jaar, Furth, Hermann, and Briggs (1999) studied a longitudinal cohort over 7 years from hospitalization and death records; 11.7% of 4,005 hemodialysis patients were found to have at least one episode of septicemia. Older age and diabetes were identified as independent risk factors. Among the hemodialysis patients, low serum albumin was also associated with increased risk. Traniover et al., (2000) reported in their study comparing two treatment strategies for bacteremia associated with tunneled dialysis catheters that patients with hypoalbuminemia were at increased risk of infection. Serum albumin is reported to be a good predictor of morbidity and mortality (Wells, 2003). Malnutrition increases as renal failure progresses. It is the outcome of inadequate dietary protein, calories, minerals, vitamins, trace elements, and other substances such as L-carnitine. In this study, the albumin levels were between 19 and 45 g/L, with a mean of 31.69 g/L. Normal serum albumin ranges from

Table 4
Skin Colonization of Exit Sites

Colonization	Group (n)		Total	*p* value
	Chlorhexidine	ExSept®		.069
> 15 cfu	56	55	111	
<15 cfu	8	2	10	
Total	64	57	121	

* cfu denotes colony forming units

Table 5
Factors Affecting Catheter-Related Infections: Immunosuppression

			Total	*p* value
Immunosuppressed	**Yes**	**No**		
Exit Site Infections (n)				1.0
Yes	0	10	10	
No	10	101	111	
Total	10	111	121	
Skin Colonization (n)				.193
Yes	8	103	111	
No	2	8	10	
Total	10	111	121	
Bacteremia (n)				*
Yes	0	2	2	
No	112	7	119	
Total	112	9	121	

* not computed

30-50 g/L. It is evident that the patients were in the low normal range and therefore could potentially be at risk for increased infection. Of the10 patients who did develop exit site infections, 6 were diabetics, 3 were hypertensive, and one patient had multiple myeloma. Six patients were between 72 and 77 years of age, one patient was 50 years, one was 60 years, and one was 83 years of age. Diabetes and older age was not associated with infection rates.

Ten of 121 patients in this study were receiving immunosuppressive therapy for various organ transplants; 7 in the Chlorhexidine group and 3 in the ExSept® group. None of the 10 patients who did develop exit site infections were taking immunosuppressive medications, but one patient who did develop an exit site infection was in ESRD secondary to multiple myeloma. There was no statistically significant difference between the groups taking or those who were not taking immunosuppressive medications in relation to the development of infection (see Table 5). In contrast, hemodialysis vascular access infection rates have also been reported by Marr et al., (1997) to be higher in immunocompromised states, such as malignancy and during the use of immunosuppressive medications.

The literature is conflicting regarding the use of prophylactic antibiotic coverage during insertion of central venous catheters. Both the National Kidney Foundation DOQI Guidelines (Laski, Pressley, Sabatini, & Wesson, 1997) and the Canadian Practice Guidelines of the Canadian Society of Nephrology (1999) do not support the use of prophylactic antibiotics. In this study there was no statistical difference between the 78 (65%) patients who received antibiotics at the time of catheter insertion and those who did not receive antibiotics in relation to catheter-related infections. Mokrzycki et al. (2000) reported that the use of prophylactic antibiotics significantly lowered the rates in exit site infections. In another study by Mavromatidis, Kontodemou, Tsoulfa, Tsorlini, and Sombolos (1999), the administration of Vancomycin did not demonstrate a reduction in catheter colonization, exit site infections, or bacteremias and recommended that administration of prophylactic antibiotics be restricted to specific groups of patients such as those taking immunosuppressants, diabetics, and patients with cancer.

Limitations of the Study

Several limitations of this study warrant review. First, the patients who participated in this study provided a good representation of patients found in hemodialysis units in Canada (CORR, 2001). The limitation is that the power required to demonstrate a significant difference between groups was limited by the size of the sample. Second, the study time was limited to 3 months per patient and/or the presence of an infection. Many infections occur within the first year. A longer study may have demonstrated other results. Third, adherence to the study protocol proved to be a challenge. More than 90 nurses from various satellite units and 121 patients were involved in the study. Though the patients all initiated dialysis in the Incenter Dialysis Unit, over time

they were transferred to satellite units. Monitoring was difficult, especially as a large number of patients were tracked by long distance communication. Staff turnover and staff-patient ratio may also have influenced consistency with the protocol. Further, staff were not blinded to the treatment solutions due to their distinctive odors. Fourth, the recorded observations were subjective. Despite orientation of more than 90 nurses to the study protocol, assessment of the symptoms of infection was variable. Last, though polysporin ointment was used consistently on all study subjects as was required by the program, the study would have been cleaner without the influence of this variable if the ointment had not been used.

Discussion

Infections are the most serious complications of tunneled, cuffed central venous catheters. Of the 121 patients participating in this study, 10 patients (8.26%) developed exit site infections; 5 were from each group. The incidence was relatively low (.91/1000 catheter days). Saad (2001) reported an incidence of exit site infections from 1.2 to 2.2 per 1000 catheter days. The exit site infections occurred at various times during the study period. The longer the catheter is in situ, the greater the possibility of catheter colonization resulting in infection (Koch, Coyne, Hoppe-Bauer, & Vesely, 2002). Each of the study patients was monitored for 3 months. A longer study period of 6 to 12 months per patient may have provided more information in relation to exit site infections and the efficacy of the antiseptics.

Two proven episodes of bacteremia occurred in this study, one per group. The literature reports that the rates vary from .15 to 3.9/1000 catheter days (Saad, 2001). The source of bacteremia is unknown; however, the possible routes of catheter contamination have been discussed extensively in the literature (Sitges-Serra, Pi-Suner, Garces, & Segura, 1995). In long-term dialysis catheters, it has been suggested that contamination may occur as a result of frequent manipulations of the catheter hub, allowing microorganisms to migrate from the hub to the catheter tip via the endolumen of the catheter. Catheter brushings or aspirate from the lumen of the catheter could provide information concerning the microorganisms that potentially cause catheter colonization, the time in which colonization occurs, and the resulting catheter-related infection (Koch et al., 2002).

It was interesting to note that although the incidence of skin colonization was high, only 10 exit site infections were observed. Of the 10 exit site infections, all had colonization of the skin surface. The microorganism primarily responsible for colonizing the skin surface was *Coagulase-negative Staphylococcus* in all 10 patients. Miller and O'Grady (2003) related that the pooled data from 1992 to 1999 indicate that *Coagulase-negative Staphylococcus* are now the most frequent causes of blood stream infections in hospitalized patients with CVCs. Of the 4 patients who were described as having bacteremia in this study, one grew *Citrobacter Freundii* in 3 of 3 vials and grew *Coagulase-negative Staphylococci* in 3 skin swabs and *Staphylococcus Aureus* on 1 skin swab. The episode of bacteremia occurred at the end of the 3-month study period. The patient was treated with antibiotics. The second patient who developed symptoms and an elevated white blood cell (WBC) grew *Coagulase-negative Staphylococcus* on skin swabs but nothing on blood culture. This episode of infection occurred in the first 2 weeks post catheter insertion. The patient received prophylactic antibiotics at catheter insertion. There was no evidence for the source of infection being anything other than the catheter. The catheter was therefore replaced and the patient received Cefazolin followed by Vancomycin as the second catheter may also have become infected based on the presence of symptoms and an elevated WBC. A third patient grew *Coagulase-negative Staphylococcus* at 1 month, no growth at 2 months, and then Streptococcus species at the beginning of the third month when the symptoms of infection developed, including an elevated temperature, chills, and generalized feeling of being unwell. This patient was treated with antibiotics even though there was no growth on blood culture. The fourth patient grew *Staphylococcus aureus* on blood culture and was symptomatic 9 days post-catheter insertion. This patient was not given prophylactic antibiotics at catheter insertion but was treated with Gentamicin for the bacteremia.

Conclusion

Infection is a well-documented complication of tunneled, cuffed CVCs. Many strategies have been studied in an effort to reduce the incidence of infection, including the antiseptics used to clean the catheter and skin surface around the catheter. The incidence of bacteremia in this study is too small to draw any valid conclusions, however, some interesting observations were made: (a) the use of prophylactic antibiotics did not appear to have any bearing on the subsequent development of bacteremia; (b) it is difficult to correlate the presence of skin colonization with an exit site infection, as there was a high incidence of colonization but only 10 patients who actually developed exit site infections; (c) the microorganisms in blood culture were not the same as those identified by skin swab, therefore the source of infection may have been from another site, such as by manipulation of the hub and the endoluminal pathway; (d) signs and symptoms of infection did not correlate well with the actual presence of infection; and (e) frequently the sites were documented as being reddened, yet there was no growth by culture. In conclusion, ExSept® 10% was comparable to Chlorhexidine 0.5 with 70% alcohol for the incidence of catheter-

related infections. However, ExSept® is less costly and has less catheter-associated damage such as catheter cracking. Thus, it would be beneficial to further study ExSept® as an alternative to Chlorhexidine.

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